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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,782	07/09/2001	Susan Hardin	0007/01UTL	9388
7590	03/02/2007		EXAMINER	
Robert W. Strozier ROBERT W. STROZIER, P.L.L.C. P.O. Box 429 Bellaire, TX 77402-0429			SMITH, CAROLYN L	
			ART UNIT	PAPER NUMBER
			1631	
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Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/901,782

Applicant(s)

HARDIN ET AL.

Examiner

Carolyn L. Smith

Art Unit

1631

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 February 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires 3 months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because

- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) They raise the issue of new matter (see NOTE below);
- (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See *Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: 56, 63, 70, 78 and 79.

Claim(s) rejected: 10, 13-19, 50-55, 57-62, 64-69, 71-77 and 79-99.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See *Continuation Sheet*.

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: _____.

Continuation of 3. NOTE: The proposed claims contain new limitations such as "the ability to remove a previously incorporated monomer", "either directly or through a linker", and "duration" which raise new issues that would require further consideration and/or search. The proposed claim set also presents additional claims without cancelling a corresponding number of finally rejected claims.

Continuation of 11. does NOT place the application in condition for allowance because: the proposed claim set contains amendments that would require further consideration and/or search. In addition, the proposed claim set presents additional claims without cancelling a corresponding number of finally rejected claims. Since the proposed claim set has not been entered, the objections and rejections stated in the FINAL action, mailed 11/3/06, are maintained.

Applicants submit a declaration by Susan H. Harding to antedate the Korlach et al. prior art reference. The declaration filed on 2/1/07 under 37 CFR 1.131 has been considered but is ineffective to overcome the Korlach reference. The evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Korlach reference. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897). In the instant case, the 131 declaration lacks evidence support for various limitations found in the instant claims, such as the ability to remove a previously incorporated monomer (i.e. proposed claim 10), the beta phosphate group (i.e. claim 16) or any of the specific amino acid positions where the tag is attached (i.e. claim 19). Since the declaration has not established an adequate correlation on a claim by claim basis that the Applicants possessed the invention prior to the effective filing date of the Korlach et al. reference, Korlach et al. is maintained.

Applicants summarize the history of the prosecution of this application. Applicants state they have submitted a Rule 131 declaration which has already been found unpersuasive for the reasons given above. Applicants argue that Korlach et al.'s provisional application does not disclose beta and/or gamma phosphate labeled dNTPs. This statement is moot as the filing date of Korlach et al.'s 09/572530 application (May 17, 2000) is sufficient for making the 35 USC 102(e) rejection. Applicants summarize Korlach et al.'s (May 17, 2000) application (now US 7,056,661) and argue that this application does not support using beta and/or gamma phosphate labeled dNTPs in the context of FRET detection of incorporating events. This statement is found unpersuasive as US 7,056,661 makes reference to using beta and gamma phosphate labeled dNTPs (col. 14, last paragraph to col. 15, first paragraph) and FRET (col. 26). Applicants argue that US 6,982,146 (Schneider et al.) fails to disclose labeling dNTP at the β or γ phosphate labelled dNTPs. This statement is found moot as Korlach et al. disclose these limitations (claim 66 and paragraphs 0064-0067).

Applicants submit what most researchers "believed" that nucleotides modified at the beta or gamma phosphate would not produce extension products, ordinary artisans would not "consider" such labeled nucleotides as good monomers for making a DNA strand, and ordinary artisans would not "view" beta or gamma labeled nucleotides as substrates in single molecule sequencing. These arguments have been fully considered and have not been found persuasive. Attention is directed to MPEP 2145. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

Applicants submit that their sequencing technology is based on detecting transient interactions between beta and/or gamma labeled dNTPs which is different from Korlach et al. and Schneider et al.'s sequencing technology. This statement is found unpersuasive as the instant invention is directed to a composition, not method claims. Applicants argue that citing the Korlach et al. application claims against the instant invention is not justified. This statement is found unpersuasive as the Korlach et al. reference discloses the claim limitations in the instant application, as set forth in the 35 USC 102 and 103 rejections, mailed 11/3/06.

Applicants arguments regarding the claim objection, 35 USC 112, 1st paragraph rejections, and 35 USC 112, 2nd paragraph rejections are based on proposed claim amendments which have not been entered and are therefore unpersuasive.

35 USC 102 rejection

Applicants summarize the 35 USC 102 rejection. Applicants argue that the polymerases and reverse transcriptases disclosed by Korlach et al. are not the "polymerizing agents" in the instant invention. This statement is found unpersuasive as the recited polymerizing agents encompass the polymerases and reverse transcriptases as disclosed and described by Korlach et al. Applicants argue that Korlach et al. do not use the term "polymerizing agent" or "monomer". This statement is found unpersuasive as Korlach et al. disclose "polymerizing agent" and "monomer" in their claims and disclose polymerizing enzymes, polymerase, and reverse transcriptase [(i.e. polymerizing agent) and dNTPs (monomers) in paragraph 0036]. Applicants again submit that the Korlach et al. 1999 provisional application does not disclose beta or gamma phosphate labeled nucleotides. This statement has already been found moot as described above. Applicants argue that Korlach et al. do not disclose a limitation for a polymerizing agent that lacks 3' to 5' exonuclease activity. This statement is found unpersuasive as Wisniewski et al. (page 28175, col. 2, first paragraph) and Gardner et al. (page 606, col. 1, last paragraph) recite these inherent characteristics. Applicants again submit that Korlach et al. 1999 provisional application does not disclose beta or gamma phosphate labeled nucleotides. This statement has already been found moot as described above. Applicants again summarize Korlach et al.'s (May 17, 2000) application (now US 7,056,661) and argue that this application does not support using beta and/or gamma phosphate labeled dNTPs in the context of FRET detection of incorporating events. This statement is again found unpersuasive as US 7,056,661 makes reference to using beta and gamma phosphate labeled dNTPs (col. 14, last paragraph to col. 15, first paragraph) and FRET (col. 26). Applicants argue that Korlach et al. do not disclose the 60 Angstrom limitation. This statement is found unpersuasive as Korlach et al. disclose this limitation in claim 69 and paragraph 0104. Applicants reiterate arguments that Korlach et al. do not

disclose using beta and/or gamma phosphate labeled dNTPs in the context of FRET detection of incorporating events which has already been found unpersuasive as described above. Applicants again argue that US 6,982,146 (Schneider et al.) fails to disclose labeling dNTP at the β or γ -phosphate labelled dNTPs. This statement is found moot as Korlach et al. disclose these limitations (claim 66 and paragraphs 0064-0067). Applicants list the original claims in the 17 May 2000 Korlach et al. application. Applicants reiterate arguments that Korlach et al. do not disclose using beta and/or gamma phosphate labeled dNTPs in the context of FRET detection of incorporating events which has already been found unpersuasive as described above. Applicants list original claim 1 in Korlach et al.'s May 17, 2000 application and discuss "nucleotide analog". This statement is found moot as the instant claims do not recite "nucleotide analog". Applicants reiterate previous arguments which have already been deemed unpersuasive.

35 USC 103 rejection

Applicants summarize the 35 USC 103 rejection. Applicants incorporate all of the arguments for the 35 USC102 rejection which have already been found unpersuasive for the reasons given above. Applicants argue that neither Korlach et al. nor Schneider et al. disclose where labels should be placed. This statement is found unpersuasive as Schneider et al. describe using thiol-reactive probes to generate fluorescently-labeled polymerase where the thiol (SH) groups that are present in the cysteine residues react with the fluors to yield chemically stable thioesters (col. 20, second paragraph), noting that fluorescently-labelled polymerases have high fluorescent yield and retain critical features of the polymerase thus preserving the function of the polymerase (col. 20, lines 26-32) as well as the limited distance of 10Å between a donor fluorophore on a polymerase and a target acceptor fluorophore on a nucleotide without collateral stimulation of other acceptor fluorophores (col. 9, fifth paragraph). Applicants summarize the FRET disclosure in Schneider et al. and argue that there is no disclosure in Schneider et al. as to how one goes about tagging a polymerizing agent using cysteine. This statement is found unpersuasive as Schneider et al. disclose the passage above involving cysteine. Applicants are reminded the instant claims are not method claims but rather are directed to a composition. Applicants argue that tagging a polymerase is not a random affair. These arguments have been fully considered and have not been found persuasive. Attention is directed to MPEP 2145. Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art. The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration. Applicants argue that Schneider et al. do not disclose that the polymerase lacks 3' to 5' exonuclease activity. This statement is found unpersuasive as Schneider et al. was not relied upon for this limitation in the 35 USC 103 rejection. Applicants point out that it is odd to indicate that claims 56, 63, 70, and 78 represent patentable subject matter while claims 88 and 99, which are equivalents of claims 56, 63, 70, and 78, are not. It is noted that claims 88 and 99 were not stated to be allowable if rewritten in independent form because they are currently rejected under 35 USC 112, 1st paragraph and 35 USC 112, 2nd paragraph. Applicants summarize the previous Examiner's arguments, mailed 11/3/06. Applicants reiterate some arguments which were already deemed unpersuasive.

Applicants arguments are deemed unperuaive for the reasons given above.

Carolyn S
Av 1631 examiner
3/1/07
Carolyn Smith